Recommendations of the SARS Vaccine Breakout Session

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What scientific and technical barriers must be overcome to develop a safe and effective SARS vaccine?

- Must understand the pathogenesis of SARS-Is it more like MHV vs FIPV? Immune mediated disease vs. viral pathology or both?
- Studies in humans to define the correlates/determinants of immunity in survivors-disease protective vs. predisposition genes
- Develop large and small animal models of SARS-vaccine protection studies and define the correlates of immunity to SARS-CoV- ? SARS CoV in primates; respiratory Bovine CoV; MHV
- Essential to sample/monitor the biodiversity of animal and human coronaviruses-because CoV can jump from animals to man and man to animals.

What scientific and technical barriers must be overcome to develop a safe and effective SARS vaccine?

- Immune monitoring assays-standardized assays for immune monitoring and for neutralization assays. (T cell overlapping peptides, high throughput neutralization assays)
- Understand the cellular and molecular mechanisms of cross-species infectious potential of CoV.
- Research community needs to move fast and learn from prior animal pandemics of CoV.

What scientific and technical barriers must be overcome to develop a safe and effective SARS vaccine?

- Define the SARS host receptors/co-receptors
- Structural studies of SARS proteins-if NA important, S protein crystal structure, NMR, mabs/receptor conjugates

What scientific and technical barriers must be overcome to develop a safe and effective SARS vaccine?

The empiric SARS vaccine approach: What SARS vaccine approaches should be pursued in the short term and in the long term?

- Live attenuated-multiple passages; reverse genetics; targeted RNA recombination
- Killed, inactivated
- Vectored for T cell responses-e.g. DNA prime and adenovirus/MVA boost
- Vectored for neutralizing antibody responses-DNA/Adenovirus
- Vectored/adjuvented for long lived protective immune responses
- S protein and other subunits (peptides) with new adjuvants that target TLRs

Questions for the rational approach to SARS vaccine development

- Is the disease a surface infection or result of viral dissemination or both?
- Does disease result from magnitude of infection or immunopathology?
- Is the initial infection site upper respiratory tract or enteric or both? Upper or lower RT?
- What are the correlates of protective immunity?
- What is the role of the innate/acquired immune systems in protection to SARS CoV ?
- Does immunity to reinfection follow recovery?

Are existing scientific and technical resouces adequate to expediciously make a safe and effective SARS vaccine?

- Reagent repository-standardized reagents widely available; recombinant proteins (e.g. multiple S); mabs, plasmids.
- Molecular immunology database on SARS-Compendium of T and B cell epitopes and the MHC Class I and II restricting elements.
- SARS/?Corona Virus sequence database-compendium of world wide sequences to monitor viral evolution.-tie in with biodiversity of corona viruses database.
- Need for BSL-3 facilities for live SARS virus work.

What are the clinical/regulatory/licensing issues for development of a SARS vaccine?

- Safety of a live attenuated vaccine; issue of revertants to virulence
- Issue of vaccine induced disease enhancement
- How and where will efficacy in humans be evaluated?
- For whom will the vaccine be recommended?
- What are the licensing issues/barriers?

What needs to be done to optimally organize the SARS vaccine effort ?

- Formation of a coordinated scientific collaborative network--a national/international coordinated effort- to work together to solve SARS vaccine problems and to work to move multiple vaccine strategies into clinical trials as soon as possible.
- Government-Academic-Industry Partnerships
- Teams working on intellectual property issues.
- Production facilities for vaccines for multiple simultaneous clinical trials-rapidly “fill the vaccine pipeline”

What needs to be done to optimally organize the SARS vaccine effort ?

- Inclusion of contacts/staff of regulatory agencies like the FDA in the teams or working groups.
- Begin to develop clinical trials capacity-?superimposed on existing “multitasking clinical trials units”